Groups; Number of Hydroxyl Groups.

REMARKS

CLAIM STATUS

Claims 1, 4, 5, 8-10, 18-20 and 73 are now pending in the application. Claims 1, 10 and 18 have been amended, as shown in Exhibit A.

Claims 1 and 18 were amended to more particularly point out and distinctly claim the invention. Claim 10 was amended solely to delete a couple of claim dependencies from claim 10. Claim 73 was added to incorporate the subject matter of the claim dependencies deleted from claim 10.

37 CFR 1.75(a)

In the Action, the Examiner objected to claim 10 as being in improper form. Specifically, the Examiner objected to claim 10 as being in the form of a multiple-dependent claim dependent from multiple-dependent claim 9. Applicant has amended claim 10 and added claim 73 to overcome this rejection.

35 USC 112

In the Office Action, the Examiner rejected claims 1, 4, 5, 8-10 and 18-20 section 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable a person skilled in the art to practice the invention. The Examiner more specifically recites as an initial objection (on page 2 of the Action) that "the claims do not disclose how to practice the invention." This seems wrong. The function of the claims is not to "disclose how to practice the invention"

invention" (that is the function of the description), but rather to set out the scope of protection. It is thus quite normal for claims to generalize concepts discussed in greater detail in the description, and in this case the "building", "selecting" and "modeling" steps which appear in independent claims 1 and 18 are discussed in sufficient detail in the specification to enable a person skilled in the art to practice the claimed invention. For example, modeling of descriptors is described at page 30 line 29 to page 31 line 10 of the present application, building a combinatorial library is described at page 33 lines 19 to 26, and selecting candidate molecules is described at page 34 lines 7 to 17.

On page 3 of the Action, the Examiner makes more specific objections that (i) the process of computationally determining molecular descriptors is not adequately described and (ii) the process for building a combinatorial library using molecular descriptors is not defined.

In respect of (i), for explanations of how to determine molecular descriptors the Examiner is again directed to the passage at page 30 line 29 to page 31 line 10 of the present application which discloses the specific computer software used to generate the recited descriptors, and also to the passages at page 6 lines 15 to 19 and page 16 lines 15 to 27 which provide support for a more general determination of descriptors as well as additional computer software used to chose the quality of the descriptors in terms of variability, along with the choice of descriptors to be used and the intercorrelation between the descriptors selected. Bearing in mind that the Examiner has recognized that "the skill of those in the art of molecular modeling is high" (page 4 line 1 of the Action), these passages would certainly be sufficient to enable such a skilled person to perform a molecular modeling step in which molecular descriptors are determined computationally.

In respect of (ii), the Examiner may have been confused by the "using said molecular descriptors" language that appeared in the second steps of claims 1and 18 prior to the present claim amendments. This language was introduced in the amended claims filed in response to the previous Action, but has now been deleted in amended claims 1 and 18. Furthermore, for explanations of how to build combinatorial libraries the Examiner is once again directed to the passage at page 33 lines 19 to 26, and also to the passage at page 14 line 2 to page 15 line 22. These passages describe the specific computer program used to generate a desired combinatorial explosion based on a recited consensus sequence. Also the high skill of those in the art, as recognized by the Examiner, is again relevant.

In conclusion, the description clearly provides sufficient teaching to enable the skilled person to perform the invention, and any narrowing of the independent claims (by further elaboration of the method steps) is unwarranted.

35 USC 103

Platt et al. teach that a molecule can be represented by its moment of inertia and moment of charge (multiple). However, in the approach of Platt et al. these are not descriptors which describe dynamic behavior. In particular, Platt et al. do not consider the notion of conformational variation, nor do they relate such variation to a desired activity. Rather, Platt et al. represent a molecule by its moments of inertia and reduce it to a cuboid object having time-invariant moments along its principal axes.

In contrast, by using a dynamic filter which represents constraints of conformational variations, the claimed method of the present invention can take account of variation of

molecular shape as a function of time (and optionally also temperature and pressure) for example when the molecules of interest are surrounded by several thousands of water molecules - in other words, an accurate simulation of a dynamic behavior. Thus an advantage of the present invention is that it is applicable to molecules, such as peptides, which are flexible. Furthermore, it is easy to imagine very different molecules having exactly the same moments of inertia and charge which would be indistinguishable using the technique of Platt et al. In contrast, representation of constraints of conformational variations would allow each of these different molecules to be distinguished.

In summary, the technique of Platt et al. is essentially static (which is why the imidazole molecule which is used to exemplify the technique is a small and rigid molecule) and does not encompass a dynamic filter according to the independent claims of the present application. For this reason, even if the skilled person were to combine the disclosures of Krieger and Platt et al. (and it is not admitted that he would do this) he would not arrive at the method of independent claims 1and 18.

Respectfully submitted,

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EXHIBIT A

1. (Thrice Amended). A computer-aided method for the provision, identification and description of molecules exhibiting a desired activity comprising;

a molecular modeling step in which molecular descriptors are determined computationally;

a step of building a combinatorial library of molecules [using said molecular descriptors];

a step of selecting candidate molecules which potentially exhibit said desired activity;

a filtering step whereby candidate molecules are filtered using at least one static filter representing a plurality of said molecular descriptors;

a further filtering step whereby candidate molecules are filtered using at least one dynamic filter representing constraints of conformational variations which each candidate molecule must satisfy in order to exhibit said desired activity.

10. (Thrice Amended). A computer-aided method according to [Claim 5, Claim 8 or] Claim 9 wherein the static criteria are based on physiochemical and topological descriptors at least some of which are chosen from the following descriptors: Molar Mass; Ellipsiodal Volume; Molecular Volume; Molar Refractivity; Lipophilia (LogP); Kappa 1; Kappa 2; Kappa 3; Kappa Alpha 1; Kappa Alpha 2; Kappa Alpha 3; Flexibility; Kier Chi V4; Randic Index; Balaban Index; Weiner Index; Sum of Condition E; Dipolar Moment; Number of C Atoms; Number of O Atoms; Number of N Atoms; Number of H Atoms; Total Number of Atoms; Number of Methyl Groups; Number of Ethyl Groups; Number of Amino Groups; Number of Hydroxyl Groups.

18. (Thrice Amended). A computer-aided method for the provision, identification and description of molecules exhibiting immunomodulatory activity comprising;

a step of molecular modeling in which molecular descriptors of a molecule having immunomodulatory activity are determined computationally;

a step of building a combinatorial library [using said molecular descriptors and] including molecules having said immunomodulatory activity;

a step of selecting candidate molecules which are potentially immunomodulatory;

a filtering step whereby candidate molecules are filtered using at least one static filter representing a plurality of said molecular descriptors; and

a further filtering step whereby candidate molecules are filtered using at least one dynamic filter representing constraints of conformational variations which each candidate molecule must satisfy in order to exhibit said immunomodulatory activity.